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EXAMINER

MCINTOSH III, TRAVISS C

ART UNIT PAPER NUMBER

1623

DATE MAILED: 08/10/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/972,854

Applicant(s)

BESSODES ET AL.

Examiner

Traviss C McIntosh

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 13 May 2004.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 17-29 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 17-29 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date _____.
- 4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____.
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: _____.

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DETAILED ACTION

The Amendment filed May 13, 2004 has been received, entered into the record, and carefully considered. The status of the claims is as follows:

Claims 17, 18 and 26 have been amended.

Claims 1-16 and 30-38 are canceled.

Remarks drawn to rejections of Office Action mailed September 16, 2003 include:

Claim objections: which have been overcome by applicant's amendments and have been withdrawn.

112 2nd paragraph rejections: which have been overcome in part by applicant's amendments and have been withdrawn in part.

103(a) rejection: which has been overcome by applicant's arguments and has been withdrawn.

An action on the merits of claims 17-29 is contained herein below. The text of those sections of Title 35, US Code which are not included in this action can be found in a prior Office action.

Election/Restrictions

The examiner notes that the species election which was set forth on June 2, 2003 in which applicants were required to elect a single hydrophilic substituent is hereby withdrawn. All species will be currently examined, that is, claim 17 will be examined in its entirety.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 17-29 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. *This is a new matter rejection.*

In the amendment filed May 13, 2004 applicants amended claim 17 in an effort to overcome the previously set forth 112 2nd paragraph rejection regarding compositions wherein applicants amended claim 17 to include the phrase “the composition comprises at least one pharmaceutically acceptable vehicle”. However, the original disclosure does not provide any guidance for any pharmaceutically acceptable vehicles other than topical or injectable vehicles. The changing of the scope of a claim, either by broadening or narrowing, can be construed as new matter as either is capable of changing the scope of what is claimed, and the narrower or broader group must be supported in its entirety by the specification as originally filed. As set forth supra, the original disclosure does not have support for any pharmaceutically acceptable vehicle as instantly claimed. Applicant is required to cancel the portion of the claims which states that A is “the composition comprises at least one pharmaceutically acceptable vehicle” and include that for which there is support founded in the disclosure as originally filed, or point to the portion of the original disclosure in which the support is found.

It is noted that a rejection of the claims is reviewable by the Board of Patent Appeals and Interferences.

Claims 17-29 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter that was not described in the specification in such a way to convey reasonably to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. *This is a written description rejection.* Claims 17-27 do not contain complete generic formulas for the compositions sought protection for.

The MPEP states in §2163 II 3 ii) “The written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species by actual reduction to practice, reduction to drawings, or by disclosure of relevant, identifying characteristics, i.e., structure or other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the claimed genus. See *Eli Lilly*, 119 F.3d at 1568, 43 USPQ2d at 1406.”

In the instant application, applicants are claiming compositions which optionally comprise various moieties. Moieties which are defined by the functional phrases include “hydrophilic therapeutic molecules”, “biologically active substances”, “an antigen”, “an antibody to said antigen”, “an enzyme”, “an inhibitor of said enzyme”, “a hormone”, “an antibiotic”, “an analgesic”, “a bronchodilator”, “an antimicrobial”, “an antihypertensive agent”, “a cardiovascular agent”, “an agent that acts on the central nervous system”, “an antihistamine”, “an

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antidepressant”, “a tranquilizer”, “and anticonvulsant”, “an anti-inflammatory substance”, “a stimulant”, “an antiemetic”, “a diuretic”, “an antispasmodic”, “an antischemic”, “an agent limiting cell death”, “an anticancer agent”, “an adjuvant”, and “an adjuvant” which comprises various moieties. Each of the above functional phrases represents an independent genus of compounds, which were not described by an actual reduction to practice, reduction to drawings, or by a disclosure of relevant, identifying characteristics, i.e., structure or other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficiently to show the applicant was in possession of the claimed genus.

Applicants are reminded of what the U.S. Court of Appeals Federal Circuit wrote in *University of California v. Eli Lilly and Co.* 43 USPQ2d 1398, “In claims involving chemical materials, generic formulae usually indicate with specificity what the generic claims encompass. One skilled in the art can distinguish such a formula from others and can identify many of the species that the claims encompass. Accordingly, such a formula is normally an adequate description of the claimed genus. A definition by function, as we have previously indicated, does not suffice to define the genus because it is only an indication of what the gene does, rather than what it is.” See *Fiers*, 984 F.2d at 1169-71, 25 USPQ2d at 1605-06 (discussing Amgen). “It is only a definition of a useful result rather than a definition of what achieves that result. The description requirement of the patent statute requires a description of an invention, not an indication of a result that one might achieve if one made that invention.” See *In re Wilder*, 736 F.2d 1516, 1521, 222 USPQ 369, 372-73 (Fed. Cir. 1984) (affirming rejection because the

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specification does "little more than outline goals appellants hope the claimed invention achieves and the problems the invention will hopefully ameliorate").

What are the structures of these molecules and where in the specification do Applicants teach how to make these potentially limitless structural variations of such molecules to be utilized in the claimed compositions? Case law is clear that such broad claims lack sufficient supporting description. Starting with a hormone case, which claimed a partially characterized peptide that was claimed in terms of its chemical properties, *In re Fisher*, 166 USPQ 18, the U.S.

Court of Customs and Patent Appeals, wrote:

It is apparent that such an inventor should be allowed to dominate the future patentable inventions of others where those inventions were based in some way on his teachings. Such improvements, while unobvious from his teachings, are still within his contribution, since the improvement was made possible by his work. It is equally apparent, however, that he must not be permitted to achieve this dominance by claims which are insufficiently supported and hence not in compliance with the first paragraph of 35 U.S.C. 112. That paragraph requires that the scope of the claims must bear a reasonable correlation to the scope of enablement provided by the specification to persons of ordinary skill in the art. In cases involving predictable factors, such as mechanical or electrical elements, a single embodiment provides broad enablement in the sense that, once imagined, other embodiments can be made without difficulty and their performance characteristics predicted by resort to known scientific laws. In cases involving unpredictable factors, such as most chemical reactions and physiological activity, the scope of enablement obviously varies inversely with the degree of unpredictability of the factors involved. In the present case we must conclude, on the record before us, that appellant has not enabled the preparation of ACTHs having potencies much greater than 2.3, and the claim recitations of potency of "at least 1" render the claims insufficiently supported under the first paragraph of 35 U.S.C. 112.

This concept was expanded by the U.S. Court of Appeals Federal Circuit in *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.* 18 USPQ2d 1016 in a case concerning EPO genes. Since genes

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were held to be chemicals, the principle regarding enablement applies as well to all small molecules. The court held that:

A gene is a chemical compound, albeit a complex one, and it is well established in our law that conception of a chemical compound requires that the inventor be able to define it so as to distinguish it from other materials, and to describe how to obtain it. See *Oka*, 849 F.2d at 583, 7 USPQ2d at 1171. Conception does not occur unless one has a mental picture of the structure of the chemical, or is able to define it by its method of preparation, its physical or chemical properties, or whatever characteristics sufficiently distinguish it. It is not sufficient to define it solely by its principal biological property, e.g., encoding human erythropoietin, because an alleged conception having no more specificity than that is simply a wish to know the identity of any material with that biological property. We hold that when an inventor is unable to envision the detailed constitution of a gene so as to distinguish it from other materials, as well as a method for obtaining it, conception has not been achieved until reduction to practice has occurred, i.e., until after the gene has been isolated.

These two cases were quoted with approval in *Genentech Inc v. The Wellcome Foundation Ltd.*, 31 USPQ2d 1161 by the U.S. Court of Appeals Federal Circuit, which added further in a concurring opinion “Such a claim, defining a substance only by its function, encompassing all substances that accomplish that result, is akin to a single means claim, which might fail to satisfy the definiteness requirement of 35 U.S.C Section 112. See *Fiers v. Sugano*, 984 F.2d 1164, 1171, 25 USPQ2d 1601, 1606 (Fed. Cir. 1993).”

In *Fiers v. Sugano*, 25 USPQ2d 1601, U.S. Court of Appeals Federal Circuit repeated its views concerning the propriety of defining a chemical by its function and emphasized that for all chemicals including DNA “Claiming all DNA's that achieve a result without defining what means will do so is not in compliance with the description requirement; it is an attempt to preempt the future before it has arrived.” They further required the inventor to have a “mental picture of the structure of the chemical, or is able to define it by its method of preparation, its

physical or chemical properties, or whatever characteristics sufficiently distinguish it. It is not sufficient to define it solely by its principal biological property.”

Both *Fiers v. Sugano*, 25 USPQ2d 1601 and *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.* 18 USPQ2d 1016 were quoted with approval by the U.S. Court of Appeals Federal Circuit in *Burroughs Wellcome Co. v. Barr Laboratories Inc.*, 32 USPQ2d 1915 who added, “An idea is definite and permanent when the inventor has a specific, settled idea, a particular solution to the problem at hand, not just a general goal or research plan he hopes to pursue. The conception analysis necessarily turns on the inventor's ability to describe his invention with particularity. Until he can do so, he cannot prove possession of the complete mental picture of the invention. These rules ensure that patent rights attach only when an idea is so far developed that the inventor can point to a definite, particular invention.”

As set forth supra, applicants claim compositions which comprise various functionally defined moieties. Compounds with divergent structure are known to act similarly, and compounds with similar structure are known to act divergently. Applicants have failed to disclose the structures of the moieties intended, and have failed to disclose the correlation between function set forth and structure of the moieties intended. Applicants have not shown they were in possession of the compositions which comprise the various broad genres of moieties which are set forth by their functional language, specifically, moieties which are defined by the functional phrases “hydrophilic therapeutic molecules”, “biologically active substances”, “an antigen”, “an antibody to said antigen”, “an enzyme”, “an inhibitor of said enzyme”, “a hormone”, “an antibiotic”, “an analgesic”, “a bronchodilator”, “an antimicrobial”, “an antihypertensive agent”, “a cardiovascular agent”, “an agent that acts on the central nervous

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system”, “an antihistamine”, “an antidepressant”, “a tranquilizer”, “and anticonvulsant”, “an anti-inflammatory substance”, “a stimulant”, “an antiemetic”, “a diuretic”, “an antispasmodic”, “an antischemic”, “an agent limiting cell death”, “an anticancer agent”, “an adjuvant”, and “an adjuvant” which comprises various moieties (“comprises” is open language, therefor, not a concise definition of a clear structure).

Therefore the full breadth of the claims fails to meet the written description provision of 35 U.S.C. §112, first paragraph. Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 U.S.C. §112 is severable from its enablement provision.

Claims 17-29 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 17 recites the limitation “the methylene groups” in line 7 of the claim. There is insufficient antecedent basis for this limitation in the claim. There has been no previously set forth methylene groups. It is noted, that there are previously set forth groups which comprise methylene groups, but it is unclear if applicants intend any of the previously set forth groups to be optionally replaced with amino groups.

As set forth supra, applicant’s amendment is considered to be new matter, and thus the rejection for claim 17 as being indefinite for comprising only one active agent is maintained for reasons of record. A composition must contain more than 1 agent, otherwise what is claimed is not a composition, but a compound. Applicants should add an additional agent for which there is support founded in the specification as originally filed to obviate the instant rejection.

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Claim 18 includes the limitation of “**substituted**” when referring to “an amino group that is optionally substituted” in the last line of the claim as set forth on page 3. In all instances, in the absence of the identity of moieties which are intended to be substituted, thus modifying an art recognized chemical core, described structurally or by chemical name, the identity of “substituted” would be difficult to ascertain. In the absence of said moieties, all the claims containing the term “substituted” which do not specifically disclose that which is to be substituted, are not described sufficiently to distinctly point out that which applicant intends as the invention.

The rejection of claim 18 as being drawn to a composition optionally comprising “a steroid derivative” is maintained for reasons of record. In the absence of the identity of moieties intended to modify an art recognized chemical core, described structurally or by chemical name, the identity of a derivative would be difficult to ascertain. In the absence of said moieties, the claims containing the term “derivative” are not described particularly sufficiently to distinctly point out that which applicant intends as the invention. Applicants argue that steroid derivatives are defined on page 11, line 26 – page 12, line 7 of the specification. However, the specification defines steroid derivatives as comprising “substituents **including, for example**, sterols, steroids and steroid hormones. Also, **for example**, the steroid derivatives **may be** chosen from cholesterol, cholestanol ... or alternatively dexamethasone”. It is noted that exemplification is not an explicit definition of anything. If applicants are relying on the specification for a definition, the specification must clearly set forth the definition explicitly and with reasonably clarity, deliberateness, and precision. See *Teleflex Inc. v. Ficosa North America Corp.*, 63

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USPQ2d 1374, 1381 (Fed. Cir. 2002); Rexnord Corp. v. Laitram Corp., 60 USPQ2d 1851, 1854 (Fed. Cir. 2001); and MPEP 2111.01.

Claim Rejections - 35 USC § 102

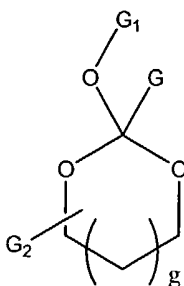
The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

Claims 17-24 and 28-29 are rejected under 35 U.S.C. 102(a) as being anticipated by Nantz et al. (US Patent 6,200,599).

Claim 17 of the instant application is drawn to a composition comprising an acid-sensitive compound which comprises a cyclic ortho-ester and a hydrophilic substituent (optionally being therapeutic molecules or optionally substituted alkyls). Claim 18 limits the acid-sensitive compound to one having the structure:



wherein g is 0-4;

G is H or 1-6C alkyl, or aryl;

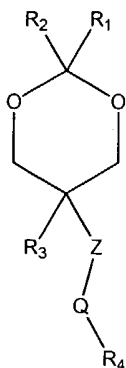
and G₁ and G₂ are selected from one being any of various hydrophilic substituents and the other being any of various hydrophobic substituents. Claim 19 provides the limitation that the

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composition additionally comprises a biologically active agent. Claim 20 limits the biologically active substance to a multitude of agents. Claim 21 provides that the composition additionally comprises an adjuvant. Claim 21 provides that the adjuvant is a neutral lipid. Claims 23-27 limit the lipid to various lipids including optionally dioleoylphosphatidylethanolamine (DOPE).

Claims 28 and 29 provide the limitation that the composition additionally comprise a vehicle for injectable formulations or topical formulations (to the skin or mucous membranes).

Nantz et al. teach of ortho-ester lipids which upon a certain pH, undergo hydrolysis with the concomitant or subsequent head group cleavage. The structural representation of the ortho-ester taught is represented by the following structure:



wherein the ring can be expanded with from 1-4 additional CH₂ moieties;

R₁ is a functional group;

R₂ is a functional group;

R₃ is a functional group;

Z is a functional group (a linker);

Q is a functional group (a cleavable group); and,

R₄ is a nitrogen-containing head group (column 2, line 45- column 3, line 19). The variable functional groups of the compound include, an ortho-ester function, a hydrophobic domain, a

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linker, a cleavable group, and a hydrophilic domain or a nitrogen head group (column 6, lines 30-34). R_1 is taught to be an alkyl chain which can be a short chain or a long chain (column 7, lines 16-18). R_2 is taught to be optionally an alkoxy group and R_3 is optionally H (column 6, lines 58-59). The compound of Nantz et al. exploits the susceptibility of the ortho ester functional group toward acid induced hydrolysis. Moreover, the putative mechanism of action for the ortho ester lipids involves structural reorganization of the lipids beyond their protonation. Acidification of ortho ester lipids results in lipid (and liposome) structural changes i.e., ortho ester conversion to an ester with headgroup cleavage and liposome disassembly. Thus, the compounds of Nantz et al. are advantageously incorporated into liposome formulations. Nantz et al. teach the liposomes to comprise the compound itself, or additionally to comprise a helper lipid, preferably non-ionic or uncharged lipids such as DOPE or cholesterol (column 9, lines 15-31). Moreover, Nantz. relates to pharmaceutical compositions comprising a lipid-nucleic acid complex which comprises a nucleic acid and their ortho-ester compound above and a pharmaceutically acceptable carrier (column 13, lines 13-22). Nantz et al. also teach to incorporate their compositions into injectable forms (column 14, lines 20-48) as well as suspending the same into a PBS buffer (can be used for topical delivery to skin) (column 23, lines 7-15). Nantz et al. disclose ortho-ester compounds which comprise a cyclic ortho-ester core, with hydrophobic and hydrophilic regions. Nantz teach that their compounds have the ability to impart advantageous properties to liposomes by programming the liposomes to disassemble in response to certain pH conditions. Nantz teach to incorporate their compounds into compositions. Nantz teach that additional agents can be complexed with, or included within their ortho-ester compounds. Applicant's invention is not seen to contain new and patentable

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distinctions over the Nantz et al. reference. Moreover, the compounds as made by Nantz et al. in the examples are seen to be the same as those claimed in the instant application. Since the Office does not have the facilities for preparing the claimed materials and comparing them with prior art inventions, the burden is on Applicant to show a novel or unobvious difference between the claimed product and the product of the prior art. See *In re Best*, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977) and *In re Fitzgerald et al.*, 619 F.2d 67, 205 USPQ 594 (CCPA 1980).

Conclusion

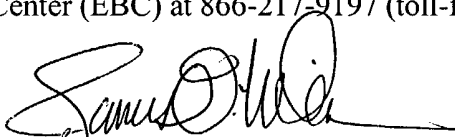
Any inquiry concerning this communication or earlier communications from the examiner should be directed to Traviss C McIntosh whose telephone number is 571-272-0657. The examiner can normally be reached on M-F 9:30-6:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James O. Wilson can be reached on 571-272-0661. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

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Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Traviss C. McIntosh III
August 5, 2004



James O. Wilson
Supervisory Patent Examiner
Art Unit 1623